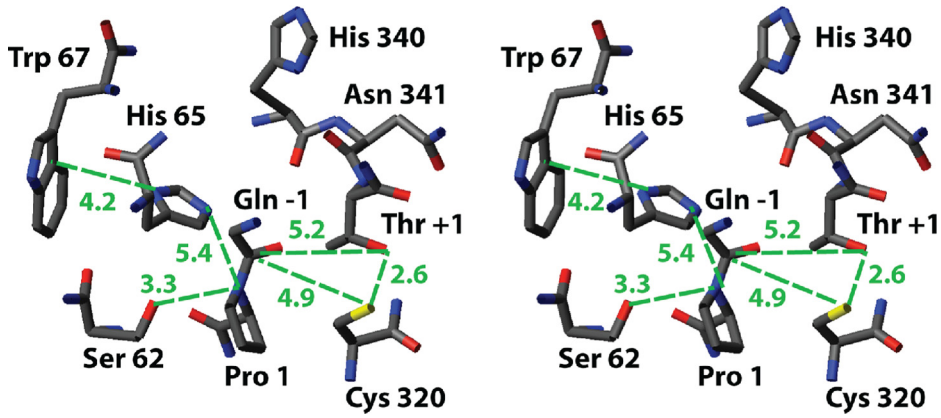
Papers of the Week

Oh Little Intein of Bethlehem ♦

♦ See referenced article, *J. Biol. Chem.* 2010, **285,** 2515–2526

Splicing of the Mycobacteriophage Bethlehem DnaB Intein. Identification of a New Mechanistic Class of Inteins That Contain an Obligate Block F Nucleophile



Stereo view of amino acid arrangement near the splice junctions in a theoretical model of the MP-Be DnaB intein; carbon atoms are colored *gray*, nitrogen atoms *blue*, and oxygen atoms *red*.

Inteins are the protein equivalent of introns, intervening peptide sequences that must be post-translationally removed from surrounding sequences, or exteins, before the protein can become functional. Like some introns, inteins are self-catalytic molecules that splice out of the host protein by means of a 4-step reaction beginning with an acyl rearrangement that forms an ester/thioester bond at the N-terminal splice junction. Several recently identified inteins, however, do not have a Cys, Ser, or Thr at the first position, making this rearrangement impossible. In this Paper of the Week, Kazuo Tori and colleagues analyzed one such intein, found in the mycobacteriophage Bethlehem DnaB protein, which begins with a structurally and chemically limiting Pro residue. However, their biochemical and mutational analysis revealed that this intein can still initiate splicing via an extremely conserved, non-contiguous Trp-Cys-Thr triplet (WCT), with the cysteine acting as the attacking residue, forming a branched intermediate structure prior to transesterification. This unusual mechanism places the DnaB intein and its relatives in a new classification known as Class 3 inteins, adding one more level to the expanding repertoire of intein-mediated splicing.

DOI 10.1074/jbc.P109.069567